Fig. 1

Fig 2

HIP1 Clones: Nucleotide Alignment

HIP1

```
        ATG                          STOP
      1 245                          2987              4796
HIP1  |─|───────────────────────────────────────────|

                                                     53%
HIP1a  876                          3058  STOP
       |───────────────────────────────|
       (3.2kb)

                                              85%
mHIP1  726                          3015  STOP
       |───────────────────────────|
       (2.3kb)

                                                     60%
          ATG
mHIP1a_195 12                       2703  STOP
          |──────────────────────────────|
          (4.0 kb)
```
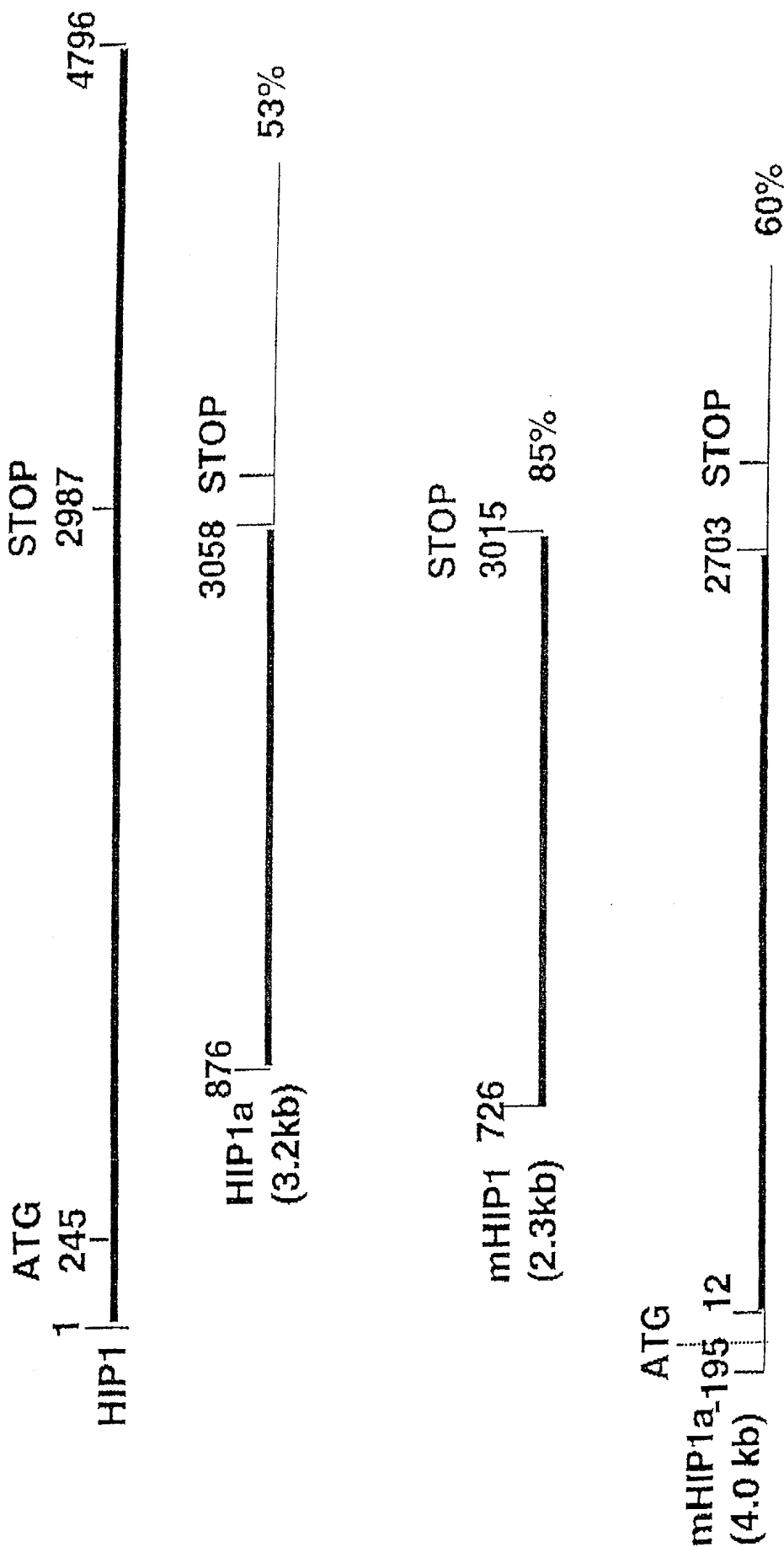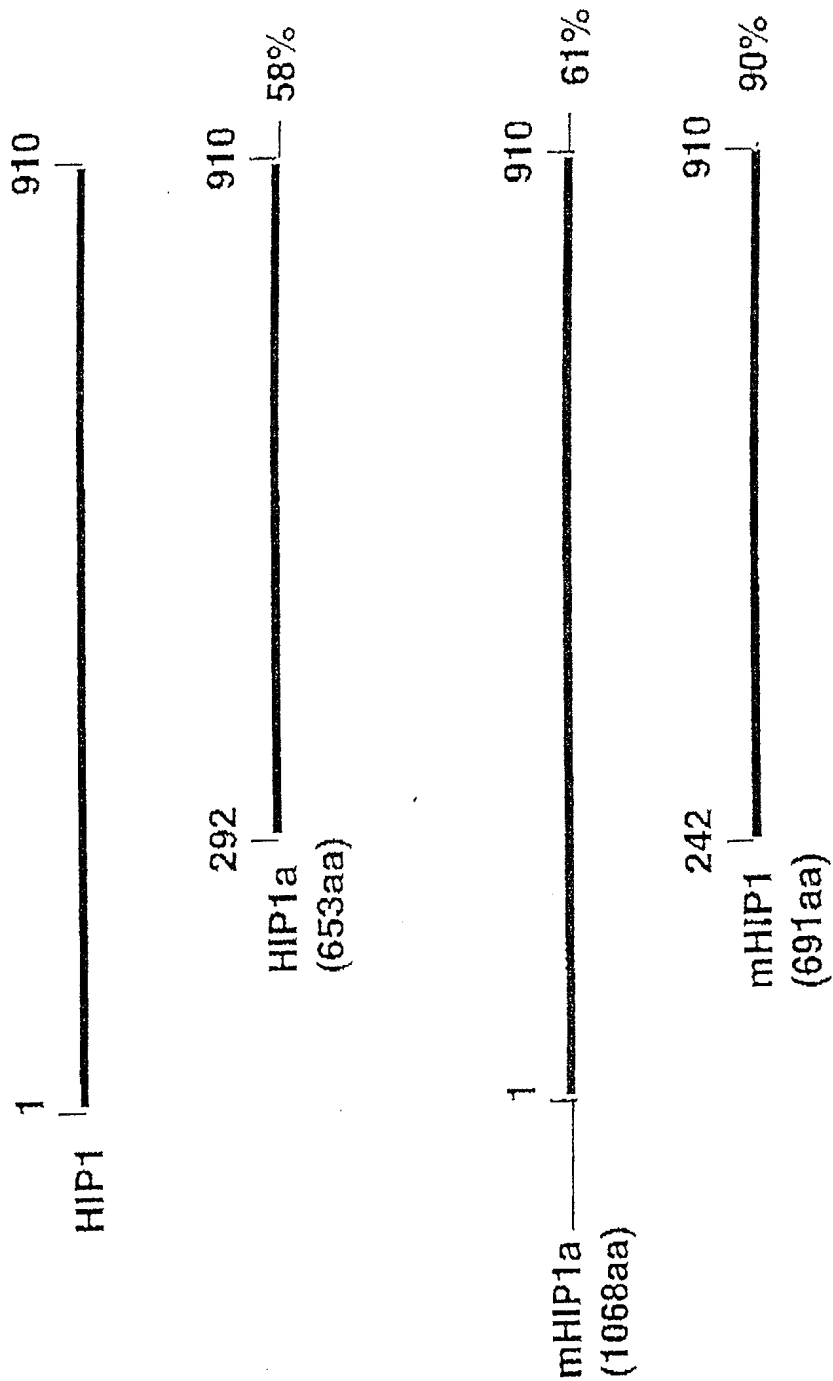
Fig 3

HIP1 Clones: Protein Alignment

Fig 4

>Usurpin A
SAEVIHQVEEALDTDEKKMLLFLCRDVAIDVVPPNVRDLLDILRERGKLSVCDLAELLYRVHRFDLLKRILK

>Usurpin B
YRVLMAHIGEDLDKSDVSSLIFLMKDYMGRGKISKHKSFLDLVVELHKLNLVAPDQLDLLEKCLKNIHRIDLKTKIQK

>Casp-8 A
FSRNLYDIGELQDSEDLASLKELSLDYIPQRKOEPIKDALMIFQRLOEKRMLEESNLSFLKELLFRINRLDLLITYLN

>Casp-8 B
YRVMLYQISEEVSREELRSFKFLLQHEISKCKLDDDMNLLDIFIEMEKRVILGEGKLDILKRVCAQINKSLLKIND

>Casp-10 A
FRHKLLTIDSNLGVQDVENLKFLCIGLVPNKKLEKSSSASDVFEHLLAHDLLSEEDPFFLAELLYIIRQKKLLQHLNC

>Casp-10 B
FRNLLYELSEGIDSENLKDMIFLLKDSLPKTEMTSLSFLAFLEKQGKIDEDNLTCLEDLCKTVVPKLLRNIEK

>FADD
FLVLLHSVSSSLSSSELTELKFLCLGRVGKRKLERVQSGLDLFSMLLEQNDLEPGHTELLRELLASLRRHDLLRRVDD

>MC159 A
SLPFLRHLLEELDSHEDSLLLFLGHDAAPGCTTVTQALCSLSQQRKLTLAALVEMLYVLQRMDLLKSRFG

>MC159 B
YHKLMVCVGEELDSSELRALRLFACNLNPSLSTALSESSRPVELVLALENVGLVSPSSVSVLADMLRTLRRLDLCQQLVE

>E8
FRCLMALVNDFLSDKEVEEHYFLCAPRLESHLEPGSKKSFLRLASLLEDLELLGGDKLTFLRHLLTTIGRADLVKNLQV

>KS orfk13A
TYEVLCEVARKLGTDDREVVLFLLNVFLPQPTLAQLIGALRALKEEGRLTFPLLAECLPRAGRRDLLRDLLH

>KS orfk13B
YQLTVLHVDGELCARDIRSLIFLSKDTIGSRSTPQTFLHNVYCMENLDLLGPTDVDALMSMLRSLSRVDLQRQVQT

>HIP1
SELEADLAEQQHLRQQAADDCEFLRAELDELRRQREDTEKAQRSLSEIERKAQANEQRYSKLKEKYSELVQNHADLLRKN
AE

>HIP1a
GELEEQRKQKQKALVDNEQLRHELAQLRAAQLERERSQGLREEAERKASATEARYNKLKEKHSELVHVHAELLRKNAD

>mHIP1a
NGLEAELEEQRKQKQKALVDNEQLRHELAQLKALQLEGARNQGLREEAERKASATEARYSKLKEKHSELINTHAELLRKN
AD

>mHIP1
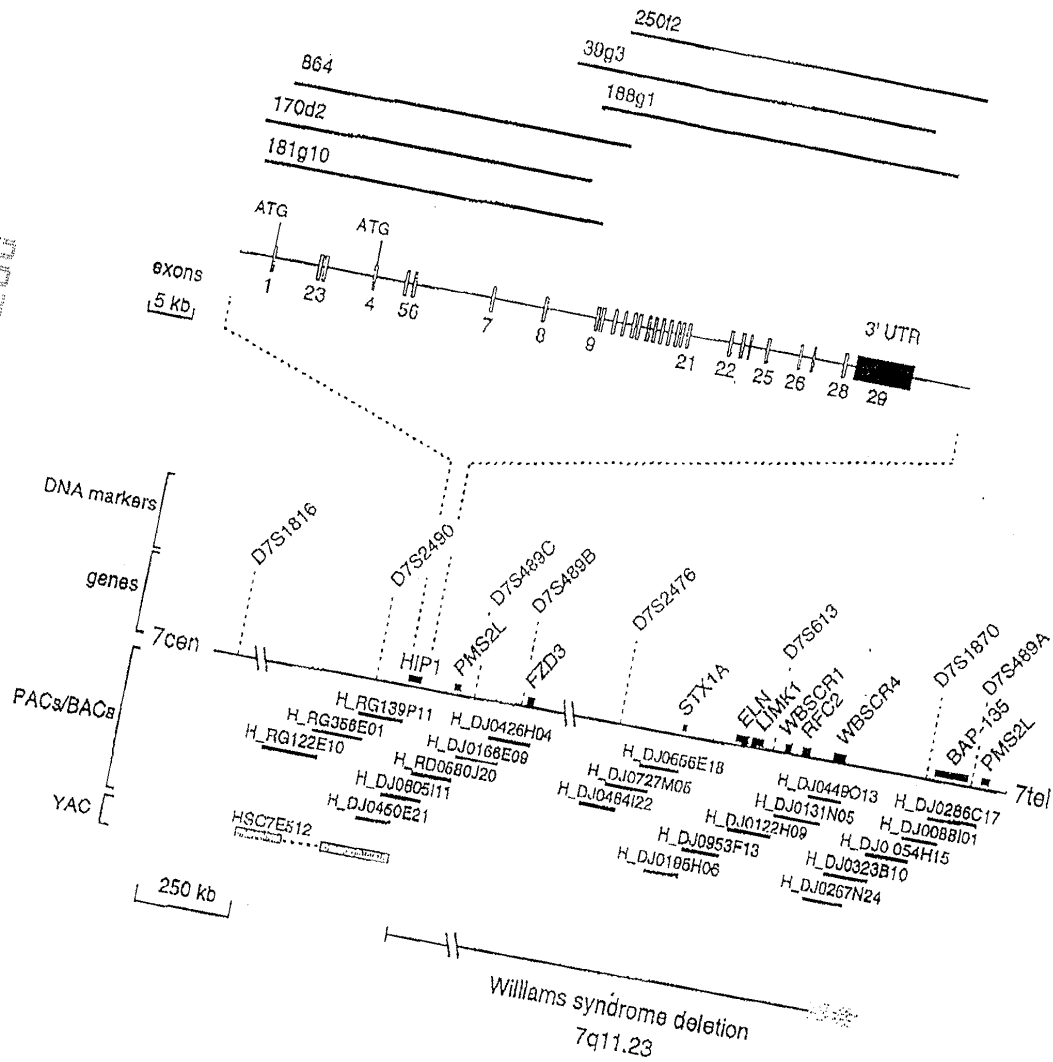SELEAELAEQQHLGRQAMDDCEFLRTELDELKRQREDTEKAQRSLTEIERKAQANEQRYSKLKEKYSELVQNHADLLRKN
AE

Fig 5

6 / 12

Fig 6

```
1 hipl     MLLCQGSEWRRDQQL GTANARQWCPLPQDA QPAGSWERCPLPPA GRLQGTDHPWGWGRL AGGGERGGLMEGLSH SQRLIHLILSLPLL           90
2 zk370.3  --------------- --------------- -------------- --------------- -------------- ----MDHRAQAREVFV          12

                Q   KAI  E       .K KHART I.GT  E KK   FK  V     L    VL KKFCH . HKLLRDGEP V        RY N      S
1 hipl     VFQTVSINKAINTQE VAVKEKHARTCILGT HHEKGAQTFHSVVNR LPLSSNAVLCWKFCH VFHKLLRDGHPNVLK DSLRYRNLSDMSRM        180
2 zk370.3  RAQLRAVQKAITQME VPLKPKHARTIIVGT EKEKLSSGIFHHTVGR IQLRKHPVLTWKFCH LVIKLLRDGHRKVPE ETYRYVNRFTQLSQP       102

                W HL   GYG     Y KLL    . HK   P PG L  D QL    KD. NF T       M       V.     R S.
1 hipl     WGHLS-EGYGQLCSI YLKLLRTKMEYHTKN PRFPGNIQMSDRQLD EAGESDVFNFFQLTV EMFDYIECEINLFQT VFNSLDMSRSVSVTA        269
2 zk370.3  WKHLNTSGYGPCIES YCKLLNDRVTFHRKY PVVPGKIDLNDSQLK TL-EGDLDWFFEMTI DMLDQHDALNVLQDR VVENRMNSLIP            191

                GQC    PLI .ILD   S   YDY VK .FKL HS .      D L G  ER RF  ? K     .   SSNLQTFK L.     IL LP   PNFL  S
1 hipl     AGQCRLAPLIQVILD CSHLYDYTVKLLPKL ESCLP-----ADTLQG ERDRFWRQ?TKLKDL FYRSSNLQTFKRLIQ IPQLPENPPNFLRAS       355
2 zk370.3  QGQCMLSPLIIAILD TSKFYDYLVKMIFKL HSQYP-----PDALEG HRSRFRTIPERTKKF YEESSNLQTFKYLVS IPTLPSHAPNTLQQS       277

                L P   R    S                          D   N D            D    I L  .    K   E
1 hipl     ALSEHISPVVVIPAE ASSPDSEPVLBKDDL MDMDASCQMLFDNKF DDIFGSSFSSDPFNF NSQNGVNKDEKDHLI ERLYRELSGLKAQLE       445
2 zk370.3  DLESYRTPHAYLHSE GS-------E----- ---DGTSLMGHRGEL LNLAEAEPQQ--ASP SSQ---FDPREEQI VMLSRAVBDEKFAKE        346

                E        .  Q                          L      E    R   T       A . E ERKA  A     R  K K  Y
1 hipl     NMKTSS---QRVVLQ LKGHVSELEADLREQ QHLRQQRADDCEFLR ARLDELRRQRRDIFK AQRSLSEIBRKAQAN EQ-RYSKLKRKYSE-       530
2 zk370.3  RLIQSA---RSRIEQ YENRLLQMQGEFDHA KREADENRFEAQRLK NELALRDASRTQTDD AR--VKEAELKATAA EE-RFNKAKGVTEK-       429

                H    L                KQ.        D          L
1 hipl     --LVQNEADLLRKN ARVTKQVSMARQAQV DLERRKKRLEDSLER ISDQGQRKTQEQLEV LRSLKQBLATSQREL QVLQGSLETSQSEA       617
2 zk370.3  --PRSREVLALTRL GDIQMQLEASEKSK? DRDEZ---ITALNR KVEEAQR---------- ------BAGRAITKA EGDAGAVD2MRTQLV       498

                F EL   D      H E      Q                AK      E   Q A      .        P
1 hipl     NHAAE?AELEKERDS LVSGAAHRBEBLSAL RKELQDTQLKLASTE ESMCQLAMDQRKHLL VGSRKAABQVIQDRL NQLEPPLIS-----       702
2 zk370.3  KADIEVEELKRTID- ------BLRESHAN- -QLVQSSAERTRKIR LAELEVAKES-GVGI TQMFDKCEDALQNAT SITYPP-----------       569

                HL            I B   LA     HL S      A      A            CK      A
1 hipl     CAGSADHLLSTVTSI SSCIEQLEKSWSQYL ACPEDISGLLHSITL LAHLTSDAIANGATT CLRAPPBPADSLTBA CKQYGRETLAYLASL       792
2 zk370.3  -------HLAQSAMRI LVNILSNER-LDBPL ATKDNV-------F AGHLLSTTLSAAASA AYTASIRSYEGVMDQ CKKV---LAAAKVAF       641

                L D        LP    DI   .    EM    AI A       IE   RA   G    LEVNE IL
1 hipl     EEGSLENADSTAMR HCLSKIKAIGEELLP RGLDIKQPELGDLVD KEHAPTSAAIBTATA RIBBMLSKSRAGDTG VXLEVNERILGCCTS        862
2 zk370.3  SDDSALSRADKHKLL RQDIQTLNSLMISLP LQTDIDKDVVGNELB QRMRRMDDAIRRAVQ BIEAIQRRARESSDG IRLEVNESILANCQA        731
```

09/701205

FIG 6 (CONT.)

```
                 EM .I L..AS  L Q EIV       SP  EFY  M  MYEGLIS A  KAVG  A V V     AD VV GRGK      F R I  V    BYAASTA
1 hip1   LMQAIQVLIVASKDL QRRIVESGRGTASPK EFYAKMSRMYEGLIS ASKAVGMGATVMVDA ADLVVQGRGK----F KELAVCSHELAASTA    958
2 zk370.3 LMSVIMQLVLASREL QTRIVAAGKGAGGSPA ERYKRMHGMTEGLLS AAKAVGVAARVLVES ADGVVIGKGI----F EHLIVALQEIAASTA    817

                 QL . S VLADKDSS  L  L  A   VRQ   TA VVA    G .       D?S  L   K  EX SQV  L ELK  L   ER KL
1 hip1   QLVAASKVRADKDSP NLAQLQQASRGVMQA TAGVVASTISGKSQI BETDM--MDFSSMTL TQIKRQEMDSQVRVL BLENKLQKERQMLGK    1056
2 zk370.3 QLFVSSPVRADKDSS KLDALSVAAKAVHQN TAQVVAVKXQCTTL NDBGS--LDFSYLSL HAAKGEMESQVKML BLEQSLMQBRAKLAA     505

                 LRK HY A .
1 hip1   LRRKHYELAGVARGW EESTEASPPTLQEVV TEKE    1090
2 zk370.3 LRKQHVRPAQLVPNK VSP---------     923
```

Fig 7
Mouse ESTs

mtthip1.pzm:Graph-2 - Tue Apr 28 11:30:41 1988

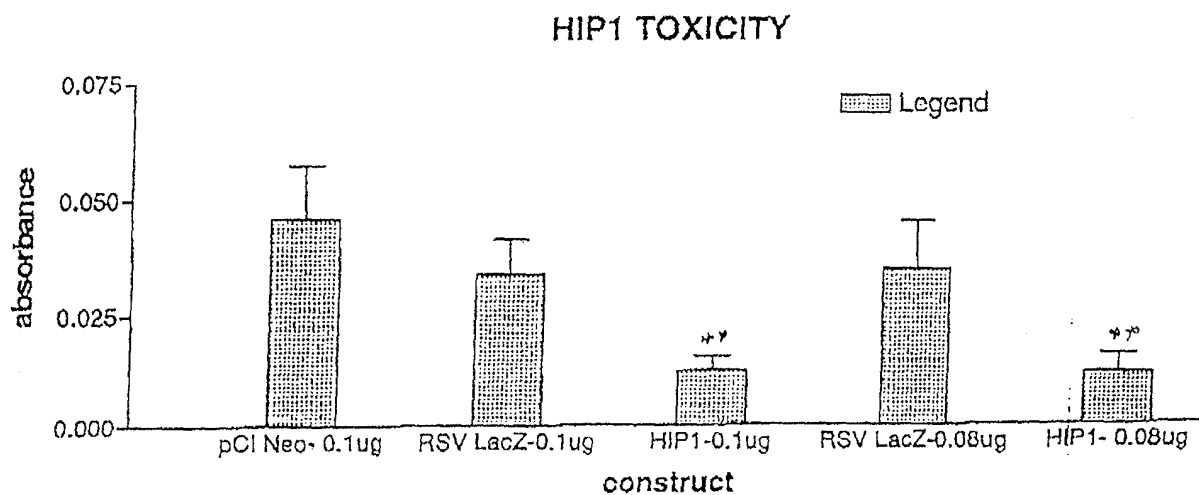_Hip-1 increases the susceptibility to cell
stress_.

HIP1 TOXICITY

Fig 8

Hip-1 is toxic in the presence of huntingtin

HIP1 transfected into HD1955-15 stable cell line
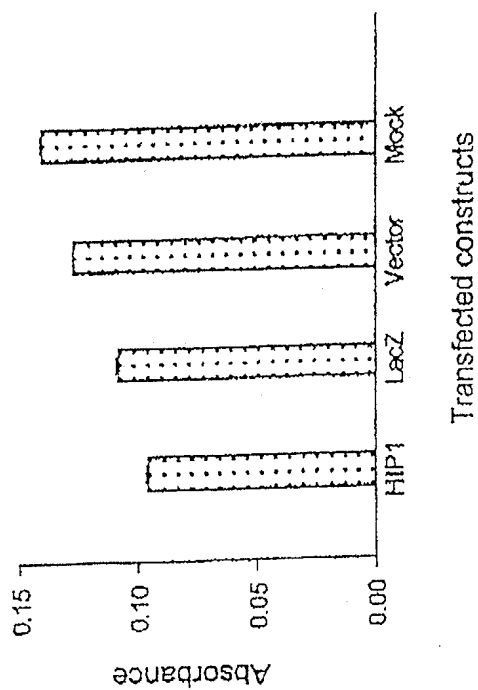36 hr post-tansfection

Fig 9A

Hip-1 is topic in the presence of huntingtin

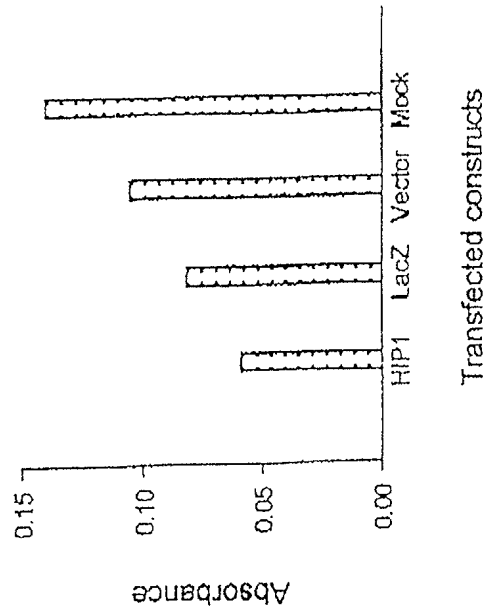## HIP1 transfected into HD1955-128 stable cell line
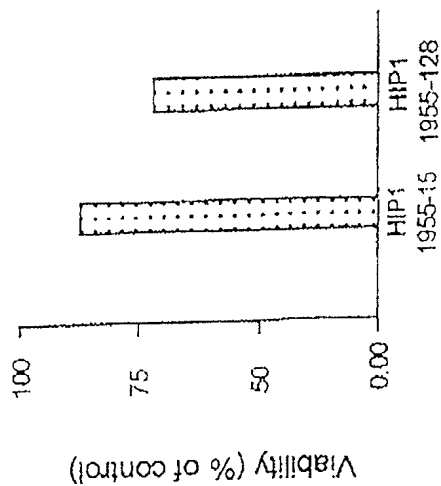## 36 hr post-transfection

Fig 9B

Polyglutamine-dependence of HIP-1 toxicity

Fig 9c

Figure: bar chart — Viability (% of control) vs. Transfected constructs/cell lines, with bars for HIP1 1955-15 and HIP1 1955-128; y-axis marked 0.00, 50, 75, 100.